Combination Nanomedicine for Overcoming Multiple Drug Resistance in Breast Cancer
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Purpose
The objective of this study was to design novel polymeric micelle-based combination therapy for treating multiple drug resistant (MDR) breast cancers.

Methods
Poly(ethylene-glycol)-block-Poly(2-methyl-2-benzoxycarbonylpropylene Carbonate) (PEG5K-PBC7K) polymers were synthesized and used for preparing doxorubicin and lapatinib loaded micelles. A film dispersion method was utilized for micelle preparation. The micelles were characterized by determining critical micelle concentration (CMC), particle size, and drug loading. In addition, the cellular uptake and anticancer effects of drug-loaded micelles were determined using a MDR breast cancer cell (MCF-7/ADR).

Results
PEG5k-PBC7k polymeric micelle had a low CMC value of around 1.5 mg/L, indicating its excellent dynamic stability. Both doxorubicin and lapatinib could be loaded into micelles with high loading efficiency at the drug/polymer ratio of 10%. The particles sizes of micelles were around 100 nm. The combination therapy with doxorubicin and lapatinib can overcome MDR and showed significant anticancer effects on MCF-7/ADR cells. Cellular uptake studies indicated that lapatinib significantly enhanced the cellular uptake of doxorubicin.

Conclusion
PEG5k-PBC7k polymeric micelles showed a low CMC value and high drug loading for both doxorubicin and lapatinib. The combination therapy with doxorubicin and lapatinib can effectively kill MDR breast cancer cells and thus has the potential to be used as a novel nanomedicine for resistant breast cancers.